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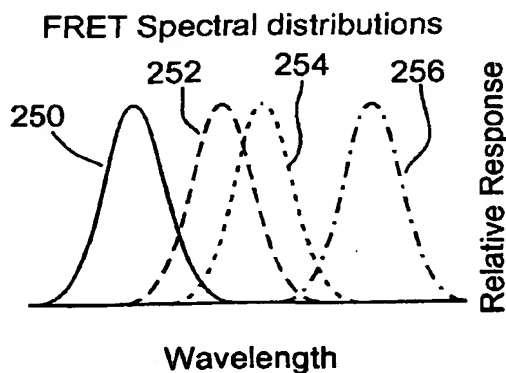
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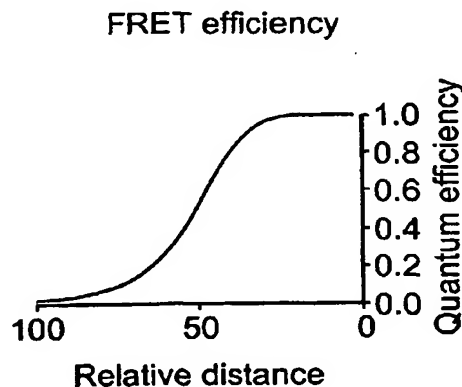
- (51) International Patent Classification⁷: C12Q 1/02, 1/48, 1/34, 1/37, 1/00, C12M 1/00, G01N 33/53
- (74) Agent: G. E. EHRLICH (1995) LTD.; 11 Menachem Begin Street, 52521 Ramat Gan (IL).
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[Continued on next page]

(54) Title: PROTEIN SYNTHESIS MONITORING (PSM)



a



b

(57) Abstract: A method and a device are disclosed for monitoring the synthesis of proteins by the ribosome in real time, *in-vivo* as well as in *in-vitro*. The ribosome is engineered to carry a donor fluorophore, and tRNA and/or amino acids and/or some other part of the ribosome are either engineered to carry acceptor fluorophores or else their natural fluorescent properties are utilized as acceptors. As the ribosome mechanism processed the mRNA and tRNA molecules and synthesizes a polypeptide chain, a light source illuminates the ribosome, exciting the donor fluorophores and thereby the acceptor fluorophores whenever these are in sufficient proximity to a donor. The resulting signals are detected and used as a key for real-time database searching and identification of the protein being synthesized. The resulting data can be tabulated and interpreted in different ways. Figure (1) describes the properties of a FRET pair and the dependence of FRET on pair distance.

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Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL03/01011

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/02, 1/48, 1/34, 1/37, 1/00; C12M 1/00; G01N 33/53
US CL : 435/29, 7.1, 15, 18, 23, 24, 4, 283.1, 968

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/29, 7.1, 15, 18, 23, 24, 4, 283.1, 968

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SEI-LIDA et al. Real-time monitoring of in vitro transcriptional RNA synthesis using fluorescence resonance energy transfer. Nucleic Acids Research. 15 June 2000, Vol. 28, No. 12, pp. E59 (Abstract Only) see entire abstract.	1-8, 32-39, 65-77, 83-86
T, &	Database DERWENT on WEST, ACC-NO:2004-487565, SMILANSKY. Abstracted-Pub-No:WO20044050825 A2, 17 June 2004 (17.06.2004), see entire abstract.	1-8, 32-39, 65-77, 83-86
Y	US 6,210,941 B1 (ROTHSCHILD et al) 03 April 2001 (03.04.2001), see entire document.	1-8, 32-39, 65-77, 83-86
Y	US 5,922,858 A (ROTHSCHILD et al) 13 July 1999 (13.07.1999), see entire document.	1-8, 32-39, 65-77, 83-86

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

18 August 2004 (18.08.2004)

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IL03/01011

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claim Nos.: 9-31, 40-64, and 78-82
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐
☐

- The additional search fees were accompanied by the applicant's protest.
No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

PCT/ISA/210

Continuation of B. FIELDS SEARCHED Item 3:

WEST/NPL: protein synthesis, marker, electromagnetic radiation, bacterial culture, rRNA, tRNA, mRNA, FRET, apparatus, amino acid, real-time